

Appl. No. 09/941,492
Reply to Office Action mailed January 24, 2005
Response dated May 24, 2005

AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

Claim 1 (Previously Presented) A cell comprising a nucleic acid molecule wherein said nucleic acid molecule comprises:

- a) one or more target binding domains that target binding of the nucleic acid molecule to a human papilloma virus pre-mRNA expressed within the cell;
 - b) a 3' splice region comprising a branch point, a pyrimidine tract and a 3' splice acceptor site;
 - c) a spacer region that separates the 3' splice region from the target binding domain; and
 - d) a nucleotide sequence to be trans-spliced to the target pre-mRNA;
- wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

Claim 2 (Previously Presented) A cell comprising a nucleic acid molecule wherein said nucleic acid molecule comprises:

- a) one or more target binding domains that target binding of the nucleic acid molecule to a human papilloma virus pre-mRNA expressed within the cell;
 - b) a 3' splice acceptor site;
 - c) a spacer region that separates the 3' splice region from the target binding domain; and
 - d) a nucleotide sequence to be trans-spliced to the target pre-mRNA;
- wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

Claim 3 (Previously Presented) A cell comprising a nucleic acid molecule wherein said nucleic acid molecule comprises:

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a) one or more target binding domains that target binding of the nucleic acid molecule to a human papilloma virus pre-mRNA expressed within the cell;
b) a 5' splice site;
c) a spacer region that separates the 5' splice site from the target binding domain;
and
d) a nucleotide sequence to be trans-spliced to the target pre-mRNA;
wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

Claim 4 (Previously Presented) The cell of claim 1 wherein the nucleic acid molecule further comprises a 5' donor site.

Claim 5 (Previously Presented) The cell of Claim 1 wherein the nucleic acid molecule further comprises a safety nucleotide sequence comprising one or more complementary sequences that bind to one or more sides of the 3' splice region.

Claim 6 (Previously Presented) The cell of Claim 1 wherein the binding of the nucleic acid molecule to the target pre-mRNA is mediated by complementary, triple helix formation, or protein-nucleic acid interaction.

Claim 7 (Previously Presented) The cell of Claim 1 wherein the nucleotide sequences to be trans-spliced to the target pre mRNA encode a human papilloma virus polypeptide.

Claim 8 (Previously Presented) The cell of claim 1 wherein the papilloma virus is an oncogenic papilloma virus.

Claim 9 (Previously Presented) A cell comprising a recombinant vector wherein said vector expresses a nucleic acid molecule comprising:

a) one or more target binding domains that target binding of the nucleic acid molecule to a human papilloma virus pre-mRNA expressed within the cell;

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- b) a 3' splice region comprising a branch point, a pyrimidine tract and a 3' splice acceptor site;
 - c) a spacer region that separates the 3' splice region from the target binding domain; and
 - d) a nucleotide sequence to be trans-spliced to the target pre-mRNA;
- wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

Claim 10 (Previously Presented) A cell comprising a recombinant vector wherein said vector expresses a nucleic acid molecule comprising:

- a) one or more target binding domains that target binding of the nucleic acid molecule to a human papilloma virus pre-mRNA expressed within the cell;
 - b) a 3' splice acceptor site;
 - c) a spacer region that separates the 3' splice region from the target binding domain; and
 - d) a nucleotide sequence to be trans-spliced to the target pre-mRNA;
- wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

Claim 11 (Previously Presented) A cell comprising a recombinant vector wherein said vector expresses a nucleic acid molecule comprising:

- a) one or more target binding domains that target binding of the nucleic acid molecule to a human papilloma virus pre-mRNA expressed within the cell;
 - b) a 5' splice site;
 - c) a spacer region that separates the 5' splice site from the target binding domain; and
 - d) a nucleotide sequence to be trans-spliced to the target pre-mRNA;
- wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

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Claim 12 (Previously Presented) The cell of claim 9 wherein the nucleic acid molecule further comprises a 5' donor site.

Claim 13 (Previously Presented) A method of producing a chimeric RNA molecule in a cell comprising:

contacting a target pre-mRNA expressed in the cell with a nucleic acid molecule recognized by nuclear splicing components wherein said nucleic acid molecule comprises:

- a) one or more target binding domains that target binding of the nucleic acid molecule to a human papilloma virus pre-mRNA expressed within the cell;
 - b) a 3' splice region comprising a branch point, a pyrimidine tract and a 3' splice acceptor site;
 - c) a spacer region that separates the 3' splice region from the target binding domain; and
 - d) a nucleotide sequence to be trans-spliced to the target pre-mRNA;
- under conditions in which a portion of the nucleic acid molecule is trans-spliced to a portion of the target pre-mRNA to form a chimeric RNA within the cell.

Claim 14 (Previously Presented) A method of producing a chimeric RNA molecule in a cell comprising:

contacting a target pre-mRNA expressed in the cell with a nucleic acid molecule recognized by nuclear splicing components wherein said nucleic acid molecule comprises:

- a) one or more target binding domains that target binding of the nucleic acid molecule to a human papilloma virus pre-mRNA expressed within the cell;
- b) a 3' splice acceptor site;
- c) a spacer region that separates the 3' splice region from the target binding domain; and
- d) a nucleotide sequence to be trans-spliced to the target pre-mRNA; under conditions in which a portion of the nucleic acid molecule is trans-spliced to a portion of the target pre-mRNA to form a chimeric RNA within the cell.

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Claim 15 (Previously Presented) A method of producing a chimeric RNA molecule in a cell comprising:

contacting a target pre-mRNA expressed within the cell with a nucleic acid molecule recognized by nuclear splicing components wherein said nucleic acid molecule comprises:

- a) one or more target binding domains that target binding of the nucleic acid molecule to a human papilloma virus pre-mRNA expressed within the cell;
 - b) a 5' splice site;
 - c) a spacer region that separates the 5' splice site from the target binding domain;
- and

- d) a nucleotide sequence to be trans-spliced to the target pre-mRNA;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

Claim 16 (Previously Presented) A method of claim 13 wherein the nucleic acid molecule further comprises a 5' donor site.

Claim 17 (Previously Presented) The method of claim 13, wherein the chimeric RNA molecule comprises sequences encoding a translatable protein.

Claim 18 (Previously Presented) A nucleic acid molecule comprising:

- a) one or more target binding domains that target binding of the nucleic acid molecule to a human papilloma virus pre-mRNA expressed within the cell;
- b) a 3' splice region comprising a branch point, a pyrimidine tract and a 3' splice acceptor site;
- c) a spacer region that separates the 3' splice region from the target binding domain;
- d) a safety sequence comprising one or more complementary sequences that bind to one or both sides of the 3' splice site; and
- e) a nucleotide sequence to be trans-spliced to the target pre-mRNA;

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wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

Claim 19 (Previously Presented) A nucleic acid molecule comprising:

- a) one or more target binding domains that target binding of the nucleic acid molecule to a human papilloma virus pre-mRNA expressed within the cell;
 - b) a 3' splice acceptor site;
 - c) a spacer region that separates the 3' splice region from the target binding domain;
 - d) a safety sequence comprising one or more complementary sequences that bind to one or both sides of the 3' splice site; and
 - e) a nucleotide sequence to be trans-spliced to the target pre-mRNA;
- wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

Claim 20 (Previously Presented) A nucleic acid molecule comprising:

- a) one or more target binding domains that target binding of the nucleic acid molecule to a human papilloma virus pre-mRNA expressed within the cell;
 - b) a 5' splice site;
 - c) a spacer region that separates the 5' splice site from the target binding domain;
 - d) a safety sequence comprising one or more complementary sequences that bind to one or both sides of the 5' splice site; and
 - e) a nucleotide sequence to be *trans*-spliced to the target pre-mRNA;
- wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

Claim 21 (Previously Presented) The nucleic acid molecule of claim 18 wherein the nucleic acid molecule further comprises a 5' donor site.

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Claim 22 (Previously Presented) The nucleic acid molecule of claim 18 wherein the binding of the nucleic acid molecule to the target pre-mRNA is mediated by complementary, triple helix formation, or protein-nucleic acid interaction.

Claim 23 (Previously Presented) The nucleic acid molecule of claim 18 wherein the nucleotide to be *trans*-spliced to the target pre-mRNA encodes a translatable papilloma virus polypeptide and/or a marker protein.

Claim 24 (Previously Presented) The nucleic acid molecule of claim 18 wherein the papilloma virus is an oncogenic papilloma virus.

Claim 25 (Previously Presented) The nucleic acid molecule of claim 24 wherein the papilloma virus is papilloma virus 16.

Claim 26 (Previously Presented) The nucleic acid molecule of claim 20 wherein the papilloma virus is an oncogenic papilloma virus.

Claim 27 (Previously Presented) The nucleic acid molecule of claim 20 wherein the human papilloma virus is an oncogenic virus.

Claim 28 (Previously Presented) A eukaryotic expression vector wherein said vector expresses a nucleic acid molecule comprising:

- a) one or more target binding domains that target binding of the nucleic acid molecule to a human papilloma virus protein pre-mRNA expressed within the cell;
- b) a 3' splice region comprising a branch point, a pyrimidine tract and a 3' splice acceptor site;
- c) a spacer region that separates the 3' splice region from the target binding domain; and
- d) a nucleotide sequence to be *trans*-spliced to the target pre-mRNA; wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

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Claim 29 (Previously Presented) A eukaryotic expression vector wherein said vector expresses a nucleic acid molecule comprising:

- a) one or more target binding domains that target binding of the nucleic acid molecule to human papilloma virus protein pre-mRNA expressed within the cell;
 - b) a 3' splice acceptor site;
 - c) a spacer region that separates the 3' splice region from the target binding domain; and
 - d) a nucleotide sequence to be trans-spliced to the target pre-mRNA;
- wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

Claim 30 (Previously Presented) A eukaryotic expression vector wherein said vector expresses a nucleic acid molecule comprising:

- a) one or more target binding domains that target binding of the nucleic acid molecule to a human papilloma virus protein pre-mRNA expressed within the cell;
 - b) a 5' splice site;
 - c) a spacer region that separates the 5' splice site from the target binding domain; and
 - d) a nucleotide sequence to be trans-spliced to the target pre-mRNA;
- wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

Claim 31 (Previously Presented) The vector of claim 28 wherein the nucleic acid molecule further comprises a 5' donor site.

Claim 32 (Previously Presented) The vector of claim 28 wherein said vector is a viral vector.

Claim 33 (Previously Presented) The vector of claim 32 wherein in said viral vector is an adeno-associated viral vector.

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Claim 34 (Previously Presented) A composition comprising a physiologically acceptable carrier and a nucleic acid molecule according to any of claims 28-33.

Claim 35 (Previously Presented) A cell comprising a nucleic acid molecule wherein said nucleic acid molecule comprises:

- a) one or more target binding domains that target binding of the nucleic acid molecule to a viral pre-mRNA expressed within the cell;
 - b) a 3' splice region comprising a branch point, a pyrimidine tract and a 3' splice acceptor site;
 - c) a spacer region that separates the 3' splice region from the target binding domain; and
 - d) a nucleotide sequence to be trans-spliced to the target pre-mRNA;
- wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

Claim 36 (Previously Presented) A method for inhibiting the expression of papilloma virus pre-mRNA in a subject having cervical carcinoma comprising administering to said subject a nucleic acid molecule comprising:

- a) one or more target binding domains that target binding of the nucleic acid molecule to a human papilloma virus pre-mRNA expressed within the cell; and
 - b) a nucleotide sequence to be *trans*-spliced to the target pre-mRNA;
- wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

Claim 37 (Previously Presented) A cell comprising a recombinant vector wherein said vector expresses a nucleic acid molecule comprising:

- a) one or more target binding domains that target binding of the nucleic acid molecule to a human papilloma virus pre-mRNA expressed within the cell;
- b) a 3' splice acceptor site; and
- c) a nucleotide sequence to be trans-spliced to the target pre-mRNA;

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wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

Claim 38 (Previously Presented) A cell comprising a recombinant vector wherein said vector expresses a nucleic acid molecule comprising:

- a) one or more target binding domains that target binding of the nucleic acid molecule to a human papilloma virus pre-mRNA expressed within the cell;
- b) a 5' splice site; and
- c) a nucleotide sequence to be trans-spliced to the target pre-mRNA;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

Claim 39 (Previously Presented) A method of producing a chimeric RNA molecule in a cell comprising:

contacting a target pre-mRNA expressed in the cell with a nucleic acid molecule recognized by nuclear splicing components wherein said nucleic acid molecule comprises:

- a) one or more target binding domains that target binding of the nucleic acid molecule to a human papilloma virus pre-mRNA expressed within the cell;
- b) a 3' splice acceptor site; and
- c) a nucleotide sequence to be trans-spliced to the target pre-mRNA; under conditions in which a portion of the nucleic acid molecule is trans-spliced to a portion of the target pre-mRNA to form a chimeric RNA within the cell.